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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,864	11/24/2000	David Scheinberg	D6126	4077

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,864	SCHEINBERG ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3, 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 1, 3, 7 are being examined.

The following are the remaining rejections.

REJECTION UNDER 35 USC 103

Rejection under 35 USC 103(a) of claims 1, 3, 7 pertaining to being obvious over Simonson et al, 1990, Cancer Res, 50 (3 Supp): 9855-9885, of record, in view of Kasperson, FM et al, of record, US 4,665,897, of record, and US 6,197,278 or Vieira, MR, et al, 1996, Eur J Surgical Oncology, 22(4): 331-4, and further in view of US 4,444744A remains for reasons already of record in paper of 10/21/2004.

1. Applicant argues as follows:

Applicant argues that a reasonable expectation of killing tumors of at least 1mm in size with Bi-213-labeled antibodies is only found in the instant application.

Applicant argues that a key element of the instant invention is that the specific activity must be high enough, and the dose of antibody sufficient to have one atom of the isotope deliver at least one alpha particle to each cell to which it binds. Applicant argues that such range of activity is about 0.1 mCi/mg to about 30 mCi/mg, and that generally for a B-213 labeled antibody targeted to a receptor comprising about 10,000 binding sites on the tumor cell, a minimum specific activity of 10 mCi/mg is required to provide one alpha particle into each cell, provided that the amount of antibody having

this specific activity is sufficient to saturate all the available binding sites on the tumor cells available for targeting. Applicant argues that repeated delivery would saturate the available binding sites on the next layer of tumor cells after killing the tumor cells available for targeting on the previous layer thereby killing the solid tumor.

Applicant argues that with specific activities of 3-10 mCi/mg Bi-212-labeled antibody taught by Simonson et al are insufficient to kill a tumor, because Simonson et al teach that no cure was achieved even with repeated administration. Applicant argues that the instant specification teaches that killing a tumor to achieve a cure or at least 5 year disease-free survival means that the probability of killing all tumor cells must approach 1, i.e. killing a tumor means reducing the number of tumor cells to 1 or none.

Applicant argues that the dose of the claimed antibody may be limited to an appropriate dose within the range recited in claim 7, not that any dose within the range is suitable. Applicant argues that determination of dose only is found in the claimed invention.

Applicant's arguments set forth in paper of 01/24/05 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the definition of "killing a tumor" is not found in the specification. The specification on page 19, second paragraph, discloses that "to achieve a cure (5 year disease-free survival), the **probability of killing all tumor cells** (emphasis added) must approach 1". The specification does not disclose a definition of "killing a solid tumor", or that using the claimed labeled antibody would achieve a cure of 5 year disease-free survival of solid tumor greater than 1 mm in size.

Thus "killing a solid tumor" as claimed in claims 1, 3, 7 encompasses treating a tumor, i.e. some tumor cells are killed, which is certainly taught by Simonson et al, i.e. a 56% decrease in tumor mass, which after 13 days of injection, is 3 gm in average.

Moreover, a cure of at least 5 year disease-free survival is not recited in the claims, nor is it a result found in any of the cited examples in the specification.

Further the specific activity of 10 mCi/mg Bi-212-labeled antibody taught by Simonson et al is within the range of the claimed specific activity. In addition, one would have expected the same specific activity of 10 mCi/mg Bi-213-labeled antibody would be obtained, using the labeling method of Simonson et al.

In addition, concerning the dosage of the labeled antibody necessary for delivery at least one alpha track to the tumor cell(s) upon binding of the antibody, wherein the dose is from about 0.1 mg/m^2 to about10 mg/m^2, it is noted that delivering "at least one alpha track" encompasses delivering any amount of alpha tracks, as long as it is at the minimum one single alpha track. It is further noted that to determine the "optimum dosage" is within the level of ordinary skill in the art. See In re Kronig, 190 USPQ 425.

Thus the method taught by the prior art seems to have the same key element of the instant application, i.e. high specific activity of the labeled antibody, 10 mCi/mg, which is within the range of the claimed specific activity. Further determining the dosage of the labeled antibody necessary for delivery at least one alpha track to the tumor cell(s) upon binding of the antibody is within the level of one of ordinary skill. See In re Kronig, 190 USPQ 425.

One of ordinary skill in the art would have expected that using the high specific activity labeled antibody taught by the combined art, wherein the specific activity is within the range of the claimed high specific activity, i.e. using a labeled antibody which seems to be the same as the claimed labeled antibody, the same result would be obtained, i.e. killing a solid tumor greater than 1 mm in size, in view that determining the optimum dosage of the labeled antibody to deliver at least one alpha track to the tumor cell is within the level of one of ordinary skill.

2. Applicant further argues that Simonson, Lemelson and Kasperson teach away from the claimed invention. Applicant argues that Simonson et al teach that despite a prolonged survival in some of the mice and significant reduction in tumor burden, a cure in none of them is obtained, even with a administration of 4 x 180 uCi on consecutive days to a tumor 8 days after inoculation. Applicant argues that since Lemelson teaches using a nonradioactive nuclide to label an antibody, regardless of the type of radiation or particle emitted upon activation, or that the nuclide labeled antibody may be administered repeatly, Lemenson teaches away from the high specific activity Bi-212 or Bi-231 labeled antibody, i.e. only alpha emitters per se, of the invention. Applicant argues that although Kasperson et al teach that Bi-213 is safer and easier to produce, Kasperson et al also teach that Bi-213 may have limited applicability in the treatment of solid tumors. Applicant argues that thus eventhough Kasperson do not preclude using Bi-213 for a solid tumor, one merely would be trying replacing Bi-212 with Bi-213 in view of this statement.

Applicant's arguments set forth in paper of 01/24/05 have been considered but are not deemed to be persuasive for the following reasons:

Contrary to Applicant's assertion, Simonson, Lemelson and Kasperson do not teach away from the claimed invention.

It is noted that killing a tumor as claimed encompasses treating a solid tumor greater than 1 mm in size, i.e. reducing growth of a tumor, supra.

Eventhough Simonson et al teach that the tumors are not cured, this limitation is not in the claims. It is clear however that the tumors are significantly reduced in size in the teaching of Simonson et al, i.e. similar to the claimed embodiment, and thus Simonson et al do not teach away from the claimed invention.

Moreover, US 4,665,897 (Lemelson) does not teach away from the invention. US 4,665,897 teaches repeated administration of antibody rendered radioactive, wherein the radiation includes alpha particles, to effect remission or destruction of tumors. In other words, the teaching of "repeated administration of a radioactive antibody to effect remission or destruction of tumors" would clearly apply to the claimed method, regardless whether said radioactive antibody has high specific activity or whether said radioactive antibody is Bi-212 or Bi-213. Further, although the secondary reference US 4,665,897 does not teach high specific activity Bi-212 or Bi-213-labeled antibody, the primary reference, Simonson et al, teaches treating tumors using antibody labeled with Bi-212, the specific activity of which antibody is within the range of the specific activity of the labeled antibody in the claimed method.

In addition, Kaperson et al do not teach away from the claimed invention. Although Kasperson et al teach that Bi-213 "may have limited" applicability in the treatment of solid tumors, however, this opinion seems to be only a possibility, and does not preclude the use of B-213 in treating solid tumors, especially in view of the teaching of Simonson et al that solid tumors are reduced in size by treating with Bi-212 labeled antibody, and further in view that Kasperson et al teach that Bi-213 is safer and easier to produce as compared to Bi-212.

3. Applicant argues that the secondary references US 6,197,278, Vieira, MR, et al, and US 4,444744A do not provide the teaching or suggestion lacking in Simonson et al, in combination with Kasperson et al and Lemelson et al.

This is not found to be persuasive. The teaching of Simonson et al, in combination with Kasperson et al and Lemelson et al clearly renders the claims obvious, supra. The secondary references complement the teaching of Simonson et al, in combination with Kasperson et al and Lemelson et al. From the teaching of US 6,197,278, or Vieira, MR, et al, it is clear that antibody, intravenously administered, could reach the target cells within minutes, and thus intravenous route of administration could be applied to the alpha emitters with short half-life such as Bi-212 or Bi-213 for treating solid tumors.

From the teaching of US 4,444744A, it would have been obvious to use antibodies to cancer cell surfaces, labeled by the method of Simonson et al, for cancer immunotherapy.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS
April 21, 2005